TETANUS.[1]

A STUDY OF THE NATURE, EXCITANT, LESIONS, SYMPTOMATOLOGY, AND TREATMENT OF THE DISEASE, WITH A CRITICAL SUMMARY OF THE RESULTS OF SERUM THERAPY.

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(CONCLUDED FROM PAGE 445.)

CASES TREATED BY INTRACEREBRAL INJECTIONS.

No. 1.—*Name,* Chaufard and Queun.[201] *Year,* 1898. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* compound fracture of finger. *Period of incubation,* fourteen days. *Day of first injection,* third day. *Method of administration,* intracerebral. *Amount,* 4 cubic centimetres and 130 cubic centimetres subcutaneously. *Make,* Roux. *Other treatment,* chloral. *Result,* recovery. *Remarks.* Author says absolutely no harm was done by the intracerebral injections, bearing out the expériments of Roux and Borrel on guinea-pigs.

No. 2.—*Name,* Garnier.[202] *Year,* 1898. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* varicose ulcer of leg. *Period of incubation,* unknown. *Day of first injection,* fourth day. *Method of administration,* intracerebral. *Amount,* 6 cubic centimetres = 15 cubic centimetres, also 30 cubic centimetres intravenously and 80 cubic centimetres subcutaneously. *Make,* Roux. *Other treatment,* chloral. *Result,* recovery. *Remarks.* Author says apparently a mild case in the beginning, but became bad later on. The intracerebral injections did no harm.

No. 3.—*Name,* Robert.[203] *Year,* 1898. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* wound of palm, caused by a piece of bone. *Period of incubation,* unknown. *Day of first injection,* first day. *Method of administration,* intracerebral. *Amount,* 7 cubic centimetres = 14 cubic

[1] Read at the meeting of the New York County Medical Society, April 23, 1900.

centimetres and 40 cubic centimetres subcutaneously. *Make*, Roux. *Other treatment*, not stated. *Result*, death. *Remarks.* According to author, a very bad case.

No. 4.—*Name*, Ombredanne.[300] *Year*, 1898. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, excoriation over knee. *Period of incubation*, nine days. *Day of first injection*, fifth day. *Method of administration*, intracerebral. *Amount*, 7 cubic centimetres = 14 cubic centimetres and 60 cubic centimetres subcutaneously. *Make*, Roux. *Other treatment*, 2.0 chloral. *Result*, recovery. *Remarks.* Only 2.0 of chloral, and author, with some justification, argues that recovery was due entirely to the antitoxin.

No. 5.—*Name*, Heckel and Reynes.[301] *Year*, 1898. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, scratch injury, caused by a nail. *Period of incubation*, about seven days. *Day of first injection*, second day. *Method of administration*, intracerebral. *Amount*, 6 cubic centimetres = 12 cubic centimetres and 40 cubic centimetres subcutaneously. *Make*, Roux. *Other treatment*, not stated. *Result*, death. *Remarks.* Autopsy showed not even a trace of meningitis; and author says this failure should not speak against Roux and Borrel's method.

No. 6.—*Name*, Delmas.[302] *Year*, 1898. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, compound fracture of forearm. *Period of incubation*, seven days. *Day of first injection*, second day. *Method of administration*, intracerebral. *Amount*, not stated and 20 cubic centimetres subcutaneously. *Make*, Roux. *Other treatment*, chloral and KBr. *Result*, death.

No. 7.—*Name*, Bacaloglu.[303] *Year*, 1898. *Diagnosis*, Tetanus (?). *Nature of injury*, cause not discovered. *Period of incubation*, unknown. *Day of first injection*, first day. *Method of administration*, intracerebral. *Amount*, 5 cubic centimetres = 14 cubic centimetres and 40 cubic centimetres subcutaneously. *Make*, Roux. *Other treatment*, chloral. *Result*, death.

No. 8.—*Name*, Du Hamel.[304] *Year*, 1898. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, gunshot wound of hand. *Period of incubation*, about twelve days. *Day of first injection*, first day. *Method of administration*, intracerebral and subcutaneous. *Amount*, 6 cubic centimetres strong. *Make*, Roux. *Result*, recovery.

No. 9.—*Name*, Hue.[305] *Year*, 1898. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, compound fracture of radius; sepsis. *Period of incubation*, six days. *Day of first injection*, first day. *Method of administration*, intracerebral. *Amount*, 6 cubic centimetres strong and 20 cubic centimetres subcutaneously. *Make*, Roux. *Other treatment*, not stated. *Result*, death.

No. 10.—*Name*, Rambaud.[306] *Year*, 1898. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, laparotomy for uterine fibroid. *Period of incubation*, ten days. *Day of first injection*, first day. *Method of administration*, subcutaneous. *Amount*, 750 cubic centimetres, also 50 cubic centimetres intravenously and 6 cubic centimetres strong intracerebrally. *Make*, not stated. *Other treatment*, not stated. *Result*, recovery, but the patient

died ten days after the disappearance of all tetanus symptoms. *Remarks.* Tetanus bacilli found in the laparotomy wound. No autopsy permitted.

No. 11.—*Name,* Rambaud.[306] *Year,* 1868. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* accidental amputation of thumb by a hatchet. *Period of incubation,* seven days. *Day of first injection,* second day. *Method of administration,* intracerebral. *Amount,* not stated. *Make,* not stated. *Other treatment,* not stated. *Result,* death. *Remarks.* Death eleven hours after injection.

No. 12.—*Name,* Church.[307] *Year,* 1898. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* extensive laceration of leg. *Period of incubation,* twelve days. *Day of first injection,* seventh day. *Method of administration,* subcutaneous. *Amount,* about 375 cubic centimetres, also 25 cubic centimetres intravenously and about 120 minims. *Make,* Gibier. *Other treatment,* chloral, morphine, antistreptococcus serum, etc. *Result,* recovery. *Remarks.* Tetanus bacilli found in the wound.

No. 13.—*Name,* Follet.[308] *Year,* 1898. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* compound fracture of foot, caused by wagon wheel. *Period of incubation,* eleven days. *Day of first injection,* second day. *Method of administration,* intracerebral. *Amount,* 10 cubic centimetres. *Make,* Paris Institute Pasteur. *Other treatment,* various remedies. *Result,* death. *Remarks.* Autopsy of brain absolutely negative.

No. 14.—*Name,* Routier.[309] *Year,* 1898. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* contused wound of palm. *Period of incubation,* ten days. *Day of first injection,* second day. *Method of administration,* intracerebral. *Amount,* 8 cubic centimetres = 16 cubic centimetres and 100 cubic centimetres subcutaneously. *Make,* Paris Institute Pasteur. *Other treatment,* not stated. *Result,* death.

No. 15.—*Name,* Bousquet.[310] *Year,* 1898. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* crushed injury of foot. *Period of incubation,* seven days. *Day of first injection,* fourth day. *Method of administration,* intracerebral. *Amount,* not stated. *Make,* Paris Institute Pasteur. *Other treatment,* not stated. *Result,* death. *Remarks.* Death ten hours after injection; very bad case.

No. 16.—*Name,* Beurnier.[311] *Year,* 1898. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* not stated. *Period of incubation,* not stated. *Day of first injection,* not stated. *Method of administration,* intracerebral. *Amount,* 8 cubic centimetres, also subcutaneously. *Make,* Paris Institute Pasteur. *Other treatment,* chloral and morphine. *Result,* death. *Remarks.* Only a short reference found.

No. 17.—*Name,* Baudomont.[312] *Year,* 1898. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* not stated. *Period of incubation,* not stated. *Day of first injection,* not stated. *Method of administration,* intracerebral. *Amount,* 5 cubic centimetres. *Make,* not stated. *Other treatment,* not stated. *Result,* death.

No. 18.—*Name,* Forgue and Roger.[313] *Year,* 1898. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* punctured wound of finger. *Period of incubation,* about one month. *Day of first injection,* fourth day. *Method of administration,* subcutaneous. *Amount,* 110 cubic centimetres and 13

cubic centimetres intracerebrally. *Make,* Paris Institute Pasteur. *Other treatment,* chloral, bromides, morphine. *Result,* recovery. *Remarks.* Evidently a very grave case in spite of long period of incubation.

No. 19.—*Name,* v. Leyden.[214] *Year,* 1899. *Diagnosis,* Tetanus puerperalis. *Period of incubation,* ten days. *Day of first injection,* first day. *Method of administration,* subdural. *Amount,* 4.0 and 5.0 subcutaneously. *Make,* Behring and Tizzoni. *Other treatment,* chloral, morphine. *Result,* recovery.

No. 20.—*Name,* Semple.[215] *Year,* 1899. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* contusion of testes, no visible wound. *Period of incubation,* three days(?). *Day of first injection,* first day. *Method of administration,* intracerebral. *Amount,* 5 cubic centimetres = 10 cubic centimetres and 60 cubic centimetres subcutaneously. *Make,* Paris Institute Pasteur. *Other treatment,* not stated. *Result,* recovery. *Remarks.* Remarkable inasmuch as there was no visible wound to be found.

No. 21.—*Name,* Cuthbert.[216] *Year,* 1899. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* lacerated wound of leg. *Period of incubation,* ten days. *Day of first injection,* fourth day. *Method of administration,* intracerebral. *Amount,* 5.0 = 10.0 and 30 cubic centimetres subcutaneously. *Make,* Paris Institute Pasteur. *Other treatment,* morphine. *Result,* death.

No. 22.—*Name,* Lawrence.[217] *Year,* 1899. *Diagnosis,* Tetanus traumaticus. *Nature of wound,* gunshot wound of foot. *Period of incubation,* eight days. *Day of first injection,* first day. *Method of administration,* intracerebral. *Amount,* 5.0 and 50 cubic centimetres subcutaneously. *Make,* Paris Institute Pasteur. *Other treatment,* chloral, morphine, KBr, Baccelli. *Result,* recovery. *Remarks.* Author believes that the subcutaneous injections were useless, and regrets the weakness of the antitoxin. He does not place much value upon the carbolic acid injections.

No. 23.—*Name,* Gibb.[218] [219] *Year,* 1899. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* crushed injury of hand, with subsequent gangrene. *Period of incubation,* seventeen days. *Day of first injection,* first day. *Method of administration,* intracerebral. *Amount,* about 71 cubic centimetres and 10.4 cubic centimetres subcutaneously. *Make,* Paris Institute Pasteur. *Other treatment,* chloral. *Result,* recovery(?), death(?). *Remarks.* See foot-note.[1]

[1] After making general remarks about the treatment of tetanus, the author concludes as follows: The unusually large intracerebral doses of serum were given on account of the intense severity of the symptoms. Apart from a scarlatina form rash over the abdomen lasting three days the injections produced no ill effect. *There was no sepsis.* In a subsequent communication, the author reports the death of this patient more than eight weeeks after the last intracerebral injection, and says that the result of post-mortem examination leaves but little doubt that the fatal termination was directly due to the particular method of the injection. Clinically, symptoms of a cerebral abscess were noted; not operated, and patient died. Post mortem an abscess-cavity was found in each frontal lobe, with pus in the lateral ventricles and around the cerebellum; bac-

No. 24.—*Name*, A. Koeher.[220] *Year*, 1899. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, Punctured wound of toe, caused by a nail. *Period of incubation*, fifteen days. *Day of first injection*, second day. *Method of administration*, intracerebral. *Amount*, 10 cubic centimetres and 90 cubic centimetres intravenously. *Make*, not stated. *Other treatment*, chloral, morphine. *Result*, recovery. *Remarks*. Author says evidently a mild case.

No. 25.—*Name*, Leed's Infirmary.[221] *Year*, 1899. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, penetrating wound of foot. *Period of incubation*, five days. *Day of first injection*, second day. *Method of administration*, intracerebral. *Amount*, 30 cubic centimetres and 15 cubic centimetres subcutaneously. *Make*, not stated. *Other treatment*, not stated. *Result*, death.

No. 26.—*Name*, Collier.[222] *Year*, 1899. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, injury of thumb. *Period of incubation*, nine days. *Day of first injection*, first day. *Method of administration*, intracerebral. *Amount*, 10 cubic centimetres and 30 cubic centimetres subcutaneously. *Make*, Roux and British Institute of Preventive Medicine. *Other treatment*, chloral. *Result*, recovery.

No. 27.—*Name*, Gimlette.[223] *Year*, 1899. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, injury of finger. *Period of incubation*, one week. *Day of first injection*, third day. *Method of administration*, intracerebral. *Amount*, 5 cubic centimetres strong and 200 cubic centimetres subcutaneously. *Make*, not stated. *Other treatment*, KBr, chloral, morphine, hyoscyamus. *Result*, recovery. *Remarks*. Author says that but for the serum the patient would inevitably have died.

No. 28.—*Name*, Schuster.[224] *Year*, 1899. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, contusion of face. *Period of incubation*, not stated. *Day of first injection*, not stated. *Method of administration*, subdural. *Amount*, 4.0. *Make*, Tizzoni. *Other treatment*, not stated. *Result*, recovery. *Remarks*. Author says that absolutely no harm was done by intracerebral injection.

teriologically, the staphylococcus pyogenes aureus was found. Author finally remarks as follows: "Every care was taken to secure asepsis while drilling the skull and injecting the serum; the drill and needle were always boiled before use, and as sepsis was not at any time observed clinically, it seems to me difficult to believe that the source of infection was introduced with the serum; but whatever may have been the exciting cause of the sepsis, damage to the brain from the '*repeated*' (italics mine) injections would unquestionably predispose to it." In this case repeated injections were risked on account of the excessive severity of the symptoms, probably, however, it is unsafe to venture a repetition of the process in any case." It is evident to me that the infection was due to insufficient asepsis. It is difficult to make injections repeatedly aseptically, as we always have to penetrate granulation tissue, which is hardly ever surgically clean; furthermore, the finding of the staphylococcus pyogenes aureus is corroborative of the fact that the infection was from the skin.

No. 29.—*Name*, Marchand.[324] *Year*, 1899. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, crushed and lacerated wound over occiput. *Period of incubation*, seven days. *Day of first injection*, first day. *Method of administration*, intracerebral. *Amount*, 5 cubic centimetres. *Make*, Roux. *Other treatment*, KBr, chloral, morphine, and 110 cubic centimetres subcutaneously. *Result*, death. *Remarks*. Author thinks that the injections were made too late; he also says that the subcutaneous injections had no effect whatever.

No. 30.—*Name*, Pitha.[326] *Year*, 1899. *Diagnosis*, Tetanus puerperalis. *Nature of injury*, low forceps delivery, incision and suture of perineum. *Period of incubation*, five days. *Day of first injection*, first day. *Method of administration*, intracerebral. *Amount*, 2.0 and 20.0, subcutaneously. *Make*, Roux. *Other treatment*, morphine. *Result*, death.

No. 31.—*Name*, Pitha.[326] *Year*, 1899. *Diagnosis*, Tetanus puerperalis. *Nature of injury*, abortion. *Period of incubation*, nine days. *Day of first injection*, first day. *Method of administration*, intracerebral. *Amount*, 2.0 and 270 subcutaneously. *Make*, Bujwid and Roux. *Other treatment*, morphine. *Result*, death. *Remarks*. Tetanus bacilli found in extirpated uterus.

No. 32.— *Name*, Pitha.[326] *Year*, 1899. *Diagnosis*, Tetanus puerperalis. *Nature of injury*, manual extraction of placenta. *Period of incubation*, nine days. *Day of first injection*, first day. *Method of administration*, intracerebral. *Amount*, 5.0 and 10.0 subcutaneously. *Make*, Roux. *Other treatment*, morphine. *Result*, death.

No. 32.—*Name*, Pitha.[326] (Rubeska). *Year*, 1899. *Diagnosis*, Tetanus puerperalis. *Nature of injury*, forceps delivery and suture of perineum. *Period of incubation*, five days. *Day of first injection*, first day. *Method of administration*, intracerebral. *Amount*, 4.0 and 20.0 subcutaneously. *Make*, Roux. *Other treatment*, morphine, chloral. *Result*, death. *Remarks*. Tetanus bacilli found in the perineal wound, but not in the extirpated uterus.

No. 34.—*Name*, Tavel.[327] *Year*, 1899. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, compound fracture of patella, with opening of joint. *Period of incubation*, eleven days. *Day of first injection*, first day. *Method of administration*, intravenous. *Amount*, 50 cubic centimetres, also 6 cubic centimetres intracerebrally and 40 cubic centimetres subcutaneously. *Make*, Tavel. *Other treatment*, not stated. *Result*, recovery.

No. 35.—*Name*, Tavel.[327] *Year*, 1899. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, injury of foot, caused by nail. *Period of incubation*, seventeen days. *Day of first injection*, fifth day. *Method of administration*, intracerebral. *Amount*, 10 cubic centimetres and 90 cubic centimetres intravenously. *Make*, Tavel. *Other treatment*, chloral. *Result*, recovery.

No. 36.—*Name*, Julliard.[328] *Year*, 1899. *Diagnosis*, Tetanus traumaticus. *Nature of injury*, gunshot wound of thigh. *Period of incubation*, six days. *Day of first injection*, first day. *Method of administration*, intracerebral. *Amount* 4 cubic centimetres. *Make*, not stated. *Other treatment*, not stated. *Result*, death.

No. 37.—*Name,* Nimier. *Year,* 1899. *Diagnasis,* Tetanus traumaticus. *Nature af injury,* compound fracture of forearm. *Periad of incubatian,* eighteen days. *Day af first injectian,* first day. *Methad af administratian,* subcutaneous. *Amaunt,* 110 cubic centimetres and 4 cubic centimetres intracerebrally. *Make,* Paris Institute Pasteur. *Other treatment,* not stated. *Result,* death.

No. 38.—*Name,* Johnson.[329] *Year,* 1900. *Diagnasis,* Tetanus traumaticus. *Nature af injury,* scratch injury of forearm. *Periad af incubatian,* six days. *Day af first injectian,* second day. *Methad af administratian,* subcutaneous. *Amaunt,* 490 cubic centimetres and 10 cubic centimetres intracerebrally. *Make,* Parke, Davis & Co. *Other treatment,* chloral, NaBr. *Result,* recovery. *Remarks.* Author says, "No sudden curative effect of the antitoxin was to be observed; nor does it seem that any argument for or against the intracerebral injections is to be drawn from this case." No ill effect was attributed to its use.

No. 39.—*Name,* Rogers.[330] *Year,* 1900. *Diagnasis,* Tetanus traumaticus. *Nature af injury,* pistol-shot wound. *Periad of incubation,* eighteen days. *Day af first injectian,* not stated. *Methad of administration,* intracerebral. *Amaunt,* 2 vials. *Make,* New York Board of Health. *Other treatment,* not stated. *Result,* death.

No. 40.—*Name,* Kocher.[331] *Year,* 1900. *Diagnosis,* Tetanus traumaticus. *Nature af injury,* lacerated wound of scalp. *Period of incubation,* seventeen days. *Day af first injection,* sixteenth day. *Methad of administration,* intracerebral. *Amount,* 10 cubic centimetres and 80 cubic centimetres intravenously. *Make,* Bernese make. *Other treatment,* chloral, morphine, Baccelli. *Result,* recovery.

No. 41.—*Name,* Kocher.[331] *Year,* 1900. *Diagnasis,* Tetanus traumaticus. *Nature af injury,* lacerated wound of eyelid. *Periad of incubatian,* six days. *Day of first injectian,* first day. *Methad of administratian,* intracerebral. *Amaunt,* 10 cubic centimetres. *Make,* Bernese make. *Other treatment,* chloral, morphine. *Result,* death. *Remarks.* Tetanus bacilli found in the wound. No injury of brain found at autopsy.

No. 42.—*Name,* Laplace.[332] *Year,* 1900. *Diagnasis,* Tetanus traumaticus. *Nature af injury,* punctured wound of foot, caused by a rusty nail. *Periad af incubatian,* ten days. *Day af first injectian,* fifth day. *Methad af administratian,* subdural in head. *Amaunt,* 60 cubic centimetres. *Make,* Paris Institute Pasteur. *Other treatment,* Baccelli. *Result,* recovery.

No. 43.—*Name,* Abbe.[333] *Year,* 1900. *Diagnasis,* Tetanus traumaticus. *Nature af injury,* toy-pistol injury of palm. *Periad af incubatian,* seven days. *Day af first injectian,* second day. *Methad af administratian,* intracerebral. *Amaunt,* 6.0 twice, and subcutaneously amount not stated. *Make,* New York Board of Health and Parke, Davis & Co. *Other treatment,* morphine, chloral, KBr. *Result,* recovery. *Remarks.* Case was complicated by a pneumonia.

No. 44.—*Name,* Abbe.[333] *Year,* 1900. *Diagnosis,* Tetanus traumaticus. *Nature af injury,* toy-pistol injury of palm. *Periad af incubatian,* eight days. *Day of first injection,* first day. *Method of administratian,*

intracerebral. *Amount,* 3 cubic centimetres and 57 cubic centimetres New York Board of Health and Parke, Davis & Co. *Other treatment,* chloral and bromides. *Result,* death. *Remarks.* Author says this case was of a severe type. Though it was injected promptly, no benefit was shown from the operation.

No. 45.—*Name,* Abbe.[833] *Year,* 1900. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* toy-pistol injury of hip. *Period of incubation,* nine days. *Day of first injection,* fifth day. *Method of administration,* intracerebral. *Amount,* 6 cubic centimetres and subcutaneously exact amount not stated. *Make,* Parke, Davis & Co. *Other treatment,* chloral, bromides. *Result,* recovery. *Remarks.* In this case improvement was noted soon after the first injection, and continued until recovery. The injection was done under cocaine and was well borne.

No. 46.—*Name,* Abbe.[833] *Year,* 1900. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* toy-pistol injury of finger. *Period of incubation,* sixteen days. *Day of first injection,* twelfth day(?). *Method of administration,* intracerebral. *Amount,* 8 cubic centimetres, and subcutaneously exact amount not stated. *Make,* Parke, Davis & Co. *Other treatment,* chloral, bromides, morphine. *Result,* death. *Remarks.* Author says no benefit was derived from the operation; but it was a bad case, and brought too late to the hospital.

No. 47.—*Name,* Abbe.[833] *Year,* 1900. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* punctured wound of foot, caused by a nail. *Period of incubation,* nineteen days. *Day of first injection,* third day. *Method of administration,* subcutaneous. *Amount,* exact amount not stated, and 6 cubic centimetres intracerebrally. *Make,* Parke, Davis & Co. *Other treatment,* bromides. *Result,* recovery.

No. 48.—*Name,* Moscheowitz. *Year,* 1900. *Diagnosis,* Tetanus traumaticus. *Nature of injury,* toy-pistol injury of palm. *Period of incubation,* seven days. *Day of first injection,* first day. *Method of administration,* intravenous. *Amount,* 30 cubic centimetres and 5 cubic centimetres intracerebrally. *Make,* Paris Institute Pasteur. *Other treatment,* chloral, bromides, morphine. *Result,* death.[1]

Of 1 case with a period of incubation of 3 days, 1 recovered and 0 died, 0 per cent; of 3 cases with a period of incubation of 5 days, 0 recovered and 3 died, 100 per cent.; of 4 cases with a period of incubation of 6 days, 1 recovered and 3 died, 75 per cent.; of 8 cases with a period of incubation of 7 days, 2 recovered and 6 died, 75 per cent.; of 1 case with a period of incubation of 8 days, 0 recovered and 1 died, 100 per cent.; of 6 cases with a period of incubation of 9 days, 4 recovered and 2 died, 33.33 per cent.; of 5 cases with a period

[1] As this article was finished and ready for publication on April 20, 1900, the cases published subsequent to that date are not enumerated.

of incubation of 10 days, 3 recovered and 2 died, 40 per cent.; of 2 cases with a period of incubation of 11 days, 1 recovered and 1 died, 50 per cent.; of 2 cases with a period of incubation of 12 days, 2 recovered and 0 died, 0 per cent.; of 1 case with a period of incubation of 14 days, 1 recovered and 0 died, 0 per cent.; of 1 case with a period of incubation of 15 days, 1 recovered and 0 died, 0 per cent.; of 1 case with a period of incubation of 16 days, 0 recovered and 1 died, 100 per cent.; of 3 cases with a period of incubation of 17 days, 3 recovered and 0 died, 0 per cent.; of 2 cases with a period of incubation of 18 days, 0 recovered and 2 died, 100 per cent.; of 1 case with a period of incubation of 19 days, 1 recovered and 0 died, 0 per cent.; of 1 case with a period of incubation of 1 month, 1 recovered and 0 died, 0 per cent.; of 3 cases in which period of incubation is not stated, 1 recovered and 2 died, 66.66 per cent.; of 3 cases in which period of incubation is not known, 1 recovered and 2 died, 66.66 per cent.

On concentrating these intracerebral cases, according to the usually published statistics, we get following values:

Of 4 cases with a period of incubation under 5 days, 1 recovered and 3 died, 75 per cent.; of 24 cases with a period of incubation from 5-10 days, 10 recovered and 14 died, 58.33 per cent.; of 6 cases with a period of incubation from 10-15 days, 5 recovered and 1 died, 16.66 per cent.; of 8 cases with a period of incubation over 15 days, 5 recovered and 3 died, 37.5 per cent.; of 6 cases in which incubation period is not given or unknown, 2 recovered and 4 died, 66.66 per cent.

From these two lists it will readily be seen that I have been able to find in the literature reported 338 cases, treated in one way or another with antitoxin; of these 338 cases, 196 were followed by recovery and 142 were followed by death, or a mortality percentage of 42.01.[1]

Regarding the second point, *i.e.*, the rapidity of development of the symptoms, we do well to divide tetanus, according

[1] It should be noted, however, that it is certain that a much larger proportion of the recoveries from tetanus are published than of the fatalities, so that the above mortality percentage should be taken with much allowance.—EDITOR.

to Rotter,[30] into following subdivisions. Naturally, however, we must always take into consideration the important factor that in the decision of the case a great deal depends upon the personal judgment of the observer, and possibly no two observers would agree upon the class into which a case is to be placed.

(*a*) Very grave cases are those in which in the course of a few hours, or one or two days, the muscles of the entire body are involved in the highest degree; these cases give an absolutely bad prognosis.

(*b*) Grave cases; in these the tetanic symptoms may set in just as acutely as in the preceding class, but the continuous contractions of the muscles alternate with onsets of clonic and tonic convulsions; many of these cases die during these attacks of disturbances of circulation or respiration (spasm of the glottis), or they die more gradually of loss of strength.

(*c*) Medium grave cases; in these the tetanic symptoms develop in the course of from a few hours or days to six to eight weeks; then the spasms gradually disappear, while at the same time the individual attacks become more mild and diminish in frequency.

(*d*) Mild cases; these are distinguished by the fact that the symptoms come on very gradually, quite frequently with a prodromal period of a number of days, during which the patients complain only of pain, drawing, and an uncertain rigidity in the muscles. Recovery in these cases is quite frequent.

(*e*) Finally, very mild cases; in which there is only a mild trismus and rigidity of the muscles of the neck; these cases are scarcely ever fatal, though the symptoms may last even through many weeks.

Treatment.—Up to within the last decade the treatment of tetanus was entirely symptomatic; there was no rationale, and, for that matter, there could not have been any before the discovery of Tizzoni and Cattani, and Behring. The treatment up to that time had merely the one object in view, to overcome the most apparent and most distressing symptoms,

i.e., the spasms and contractions. Since the discovery of the tetanus bacillus and its toxins, and the mode of their action, the treatment has been modified to a great extent; hence, at the present date a rational treatment of tetanus would have to include the following points:

(1) To destroy the bacteria at the seat of infection and thereby prevent a further production of toxins.

(2) To eliminate from the body the toxins already absorbed from the primary lesion.

(3) To neutralize and render innocuous the poison already absorbed.

(4) To immunize the body after local infection has taken place.

(5) To overcome the symptoms induced by the action of the toxins.

1. To destroy the bacteria at the seat of infection, and thereby prevent a further production of toxins. As already stated, and found by the experiments of Kitasato, Rosenbach, and others, the bacilli of tetanus in the greatest majority of cases remain confined to the point of infection, and are not spread throughout the system; hence it is important to proceed at once surgically, to enlarge the wound and remove all foreign matter. Too much stress cannot be laid upon this point, and yet it is so self-apparent that it is and should be a *sine qua non* to every mind with the least bit of surgical training. Tetanus germs are practically found everywhere, and are so frequently carried into small wounds by bits of wood, earth, and in this country with the inevitable paper wad of the fourth of July toy-pistol, that I am fairly confident that its prompt removal alone would in many instances prevent the occurrence of tetanus. A large experience during several years at one of the largest public dispensaries of New York City has, however, led me to the belief that this first surgical rule is very frequently neglected, as I have had opportunity to remove on many occasions the bits of cartridge-wad from patients who had been under a physician's treatment before coming to the dispensary.

After removing the offending foreign body, the next step should be a thorough disinfection of the wound. This has for its object, however, not only the destruction of the tetanus bacilli, which, in their resting spore form, the form in which they most probably occur in wounds, is a most difficult thing to do, requiring long exposure to very concentrated antiseptics; but the disinfection certainly does away with the other saprophytic and pyogenic germs. It may appear trivial at first sight even to take saprophytic germs into consideration when dealing with another so virulent an infection as tetanus; but in reality it is a very important consideration, as we have learned from the experiments of Vaillard and Rouget [50] that nothing is better for the development of the tetanus germs than the co-existence of other micro-organisms.

Many disinfecting agents have been recommended; it is comparatively easy to kill the saprophytic germs, but, as it should be our aim to destroy also the tetanus bacilli, we should resort to antiseptics which are in a measure also active on the spores of the tetanus germs. Of the most frequently used and recommended as active are: (*a*) 1:1000 bichloride of mercury solution to which has been added 5 per cent. tartaric acid or 0.5 per cent. hydrochloric acid; (*b*) 2 per cent. carbolic acid solution; (*c*) 1 per cent. Kresol solution. (*d*) Sahli [67] recommends very highly tinctured iodine which contains 1 or 2 per cent. terchloride of iodine. Stronger and more sure is the cauterization of the entire wound, either with the actual cautery or with a strong solution of nitrate of silver.

The question of amputation of the injured member, if possible, should also be taken into consideration. Opinions differ very widely regarding this point; the most generally accepted opinion, however, reserves for amputation only those cases in which, in consequence of complicated and very dirty wounds, a thorough disinfection is impossible by other means; in other words, each case is governed by the general surgical rules applicable to injuries. I doubt whether anybody would amputate even a toe or a finger before any symptoms of tetanus arose.

2. To eliminate from the body the toxins already absorbed from the source of infection. It has not as yet been definitely decided through which channels the tetanus toxins are eliminated from the system. The main channel appears to be with the urinary secretion, although the experiences of various observers are still conflicting; Brunner (*loc. cit.*), Blumenthal,[58] Bruschettini,[60] taking opposite sides; the toxins have surely been found in the lacteal secretions of animals; they have not been found in the bile; and nobody has as yet succeeded in finding toxins in the perspiration. In spite of the conflicting observations, however, by analogy with other intoxications, we are justified in utilizing known methods of depletion, as diuresis, catharsis, and diaphoresis. The latter is hardly ever indicated by artificial measures, as excessive perspiration is one of the marked symptoms of tetanus.

Although I have not been able to find any reference to it in the literature at my command, one method of depletion appears to me to have a great deal to commend it; and I believe it is certainly worthy of trial, provided the condition of the patient is such as to warrant it. I base this recommendation not upon personal experience, but more upon the theoretical ground that at least in animal experiments the blood was nearly always found to contain the toxins; it may be well to perform venesection, withdraw a certain quantity of blood, and substitute for it normal saline solution.

3. To neutralize and render innocuous the poison already absorbed. This has for its fundamental principle the treatment by means of introducing into the system the serum of animals which have been rendered immune to the disease.

Behring, Tizzoni and Cattani, and Kitasato through numerous interesting experiments found that it is possible to immunize certain animals against fatal doses of the toxins, by introducing into their system hypodermatically either attenuated toxins in augmenting doses, or attenuated pure cultures of the tetanus bacillus. The blood serum of an animal immunized in this manner contains the specific antitoxin, and was found to give immunity against the specific disease to

other animals. This immunizing power is quantitatively proportionate to the amount of antitoxin present in the serum. From their interesting experiments it was also found that it is not only possible to immunize animals against infections which are to follow the immunization, but also that it is possible to avert a fatal termination in cases of infection, provided an injection of serum containing this antitoxin is made within a reasonable time; in other words, the serum of immunized animals has not only an immunizing power for healthy animals, but also a curative power in already diseased or infected animals.

The mode of action of the antitoxin, however, has not yet been acceptably explained. Some observers, as Behring and Kitasato,[60] Sahli (*loc. cit.*), and others, look upon its action as a chemical one, and base their view upon the fact that when toxins are mixed in a test-tube with the proportionately required amount of antitoxin, and if this mixture is then injected into animals to which this dose of the toxins is fatal, no tetanus arises.[1] From this experiment Behring argues that, theoretically at least, all cases of tetanus are curable, provided that a sufficient amount of antitoxin in sufficient concentration is introduced into the system to neutralize the toxins within the body. As a matter of fact, however, this theory is not based upon sufficient foundation, as the following objections might, and justly, be adduced against it; first, that we deal in the living body with conditions which materially differ from the test-tube; and, secondly, that we have seen that in the living body the toxins are fixed more or less permanently into the motor cells of the spinal cord. But, finally, Buchner [61] [62] [63] has experimentally proven the fallacy of the above theories. He came to the conclusion by noting a difference in reaction which he obtained by injecting into animals various mixtures of toxin and antitoxin. He found that the two substances do not influence each other directly in a chemi-

[1] A somewhat similar result was obtained by Calmette in his experiments with snake poison; snake poison mixed in a test-tube with the proportionate amount of antivenin, and injected into rabbits failed to produce death.

cal light, and that there does not occur a neutralization of the toxins by the antitoxins; but that both substances act only through the medium of the living body, *i.e.*, that both have a special influence upon the living organism, but in an antagonistic manner. Buchner claims that the cells already affected cannot be freed from their inherent poison, but looks upon the curative power of the antitoxin (which he does not deny) merely as an immunizing action upon such cell territories, which up to the introduction of the antitoxin into the body, have not yet been affected by the tetanus poison; so that these unaffected cells do not respond to the destructive agency of the toxins.

The latest theory regarding the action of the antitoxin is named by its proposer, Ehrlich,[334] the "side-chain" (Seitenketten) theory; and many observations have been published in support of it by Knorr,[335] Wassermann and Takaki (*loc. cit.*), Cobbet,[336] and others; though others, Buchner in particular, do not give much credence to it, and claim that it is too fanciful. To my mind it is exceedingly difficult to understand and much more difficult to explain in few words; essentially it means the following: There exists in every cell (in the case of tetanus they are the cells of the brain and spinal cord) a certain substance which renders these cells susceptible to a certain poison; but the possession of this substance gives also the power to the cell to produce the corresponding antitoxin. In other words, that portion of the cell protoplasm which has the power to combine with a given toxin Ehrlich calls the "Seitenkette" (side-chain), and, when so combined, liberates from the cell an antitoxin which is thrown into the circulation, and may be collected there. From a chemical point of view the term "Seitenkette" is identical with antitoxin.

No matter which theory regarding the action of the antitoxin is accepted as the true one, all that can be positively accepted as proven regarding its value to this point may be briefly stated in the following:

(*a*) It is possible to immunize animals by injections of attenuated toxins or attenuated cultures.

(*b*) The blood serum of such immunized animals will prevent the outbreak of tetanus in animals which are to be infected.

(*c*) The blood serum of such immunized animals can cure already infected animals, provided it is injected sufficiently early and in sufficient amount and concentration.

This can be done practically in all cases of experimental tetanus in animals. However, if we attempt to transfer and compare these results with tetanus in the human being, though we do certainly find some improvement in the statistics, it is still not to that marked degree which we should expect to find. The question arises, therefore, to what cause or causes is this difference due? It is my own personal opinion, which appears to be corroborated by the careful reading of the 338 cases commented upon in my list, that the principal cause of failure lies in our defective powers to diagnosticate tetanus sufficiently early. When we *can* make the diagnosis of tetanus, the destructive process in the spinal cord has gone on to such a degree that a complete *restitutio ad integrum* is almost an impossibility; or, as Marchand [64] so tersely says, "The patient with tetanic symptoms is not beginning to have tetanus; but is beginning to die of tetanus."

As a matter of fact, our efforts in the treatment of tetanus, when our present knowledge of the pathological anatomy is taken into consideration, should aim at the following points:

(*a*) To neutralize the toxins circulating in the body;

(*b*) To prevent their toxic effect on hitherto unaffected parts;

(*c*) To withdraw the toxins from affected cell territories.

The experiments of Kitasato and Behring (*loc. cit.*) show that with a properly executed and timely treatment with antitoxin we can do justice to the first requirement, and if we consider Buchner's hypothesis as correct, we will also fulfil the second requirement, but regarding the third point there still exists considerable doubt.

The experiments of Blumenthal (*loc. cit.*) have proven that when tetanus patients were treated with antitoxin, the blood of these patients has lost its poisonous properties; but, in spite of this beneficial action, many patients still died; this could not but lead to one conclusion, namely, that the toxins have already accumulated in one particular part, *i.e.*, the spinal cord, in sufficient amount to bring on a fatal termination. This proposition was also proven when the blood from a patient treated with antitoxin injected into mice gave rise to no tetanic symptoms, while bits of the spinal cord implanted into mice were always followed by unmistakable tetanus.

The solution of this problem therefore reduced itself to the question of our ability to introduce the antitoxin into those parts where the principal pathological lesions are found (the higher nerve centres), *i.e.*, into absolute proximity, if not actual contact, with the toxins themselves.

To do justice, also, to this question, Roux and Borrel [65] evolved the intracerebral method, and have certainly demonstrated its efficacy in animal experiments. Roux and Borrel infected forty-five guinea-pigs with tetanus, and subsequently treated them by trephining and injecting the antitoxin directly into the brain, and in this manner succeeded in saving thirty-five; while of seventeen others treated only with subcutaneous injections, only two survived; and of a further seventeen control animals, which received no treatment whatsoever, all died. The experiments of Roux and Borrel are based upon the fact that when a portion of brain substance is crushed and intimately mixed with some tetanus toxins, and this resulting mixture is then centrifugalized, it separates into two layers; the upper layer is an opalescent liquid, while the lower stratum is the nerve substance. Further research has demonstrated the fact that the upper layer contained very little or none of the toxins; while the lower or nervous substance contained all or nearly all of the toxins. Now, while these experiments go to prove merely the intimate relationship between nerve cells and toxins, it gave an impetus to their experiments, of trephining and introducing the antitoxin directly into the brain sub-

stance. The question naturally arises, Can we expect that the relatively small amount of antitoxin which we can inject into the cerebral hemispheres will become diffused sufficiently rapidly, so as to bring it into intimate contact and relation with the toxins fixed in the affected cells?

Independently of Roux and Borrel, Blumenthal and Jacob [66] saw the importance of bringing into intimate relation the antitoxin with the toxins; in other words, to introduce the antitoxin directly into the spinal cord, and in this manner evolved the subdural method as reported by Jacob.[67] Their experiments were executed on tetanized goats, which were treated at once upon the outbreak of the tetanus symptoms with subdural injections of antitoxin into the spine, but all of the animals died. They have also repeated the experiments of Roux and Borrel, but not with the almost uniformly good results which these observers have obtained. As a result of their experiments, they come to the conclusion that at the outbreak of the series of symptoms, which we designate collectively as tetanus, the tetanic poison is already so firmly fixed in the central nervous system that it is impossible to remove it therefrom, even with the aid of subdural injections; and they feel themselves obliged to warn against a too sanguine expectation of Roux and Borrel's method. It is evident, even from this short explanation, that this point of the treatment is not by any means closed, and requires further elucidation.

A research into the statistics may help us in clearing up the value of this method; but, just as is the case with statistics usually, there is always the personal equation to be contended with. No one can say whether the cases so far reported would not have done equally as well with subcutaneous injections alone. Another point which must not be overlooked, is that personal pride and human nature impel us rather to report our successes, than our failures.

To many it may very properly appear to be no trivial matter to inject three cubic centimetres or more of a foreign liquid into so important an organ as the brain. I must confess I have carried out the injection in my patient on this account

with a great amount of hesitation, and only after due deliberation. It should also not be forgotten that the fluid is injected into the comparatively unimportant anterior lobes. A revision of the cases reported regarding this point might be of some importance. In the cases reported as cured, the opinion appears to be unanimous that the injections were well borne, and were not productive of the least harm; while in the cases with a fatal termination, and upon which an autopsy was permitted, the investigation revealed no gross injury.

In Roberts's case (No. 3) the autopsy showed around the trephine opening a slight subcutaneous hæmorrhage. On the right side there was found in the pia mater an ecchymosis about the size of a pinhead, and a trifle larger one on the left side. On removing the meninges, there were found on both sides of the brain two pinpoint pricks which were almost imperceptible. On incising the brain, there was found on the left side an insignificant channel of about the diameter of a needle; while on the right side there existed a subcortical cavity about the size of a hazel-nut, which was filled with liquid blood, its walls were soft and covered with a hæmorrhagic exudate.

In Heckel and Reynes's case (No. 5) the autopsy showed no trace of meningitis; while of the punctures hardly a visible trace remained.

In Delmas's case (No. 6) the autopsy showed on the right side an abundant hæmorrhagic prick, and on the left side a cavity about the size of a small pea filled with blood.

Gibbs's case (No. 23) would to a great measure speak for the danger of intracerebral injections, but, on careful consideration, it is readily seen that too much importance should not be attached to it; the case was merely one of sepsis, caused not so much by the injection, as recommended by Roux and Borrel, but more probably through one of the later injections, through more or less infected granulation tissue. (See also remarks in the report of the case.)

In Pithas's case (No. 31) the autopsy showed on the right side of the brain merely the puncture wound, with slight hæmorrhage around it, and in addition on the left side the same state and also a small cyst containing a little bloody serum, caused by a crushing of the corresponding portion of the brain.

In Pithas's case (No. 33) the autopsy showed on the right side of the brain, along the channel of the needle, a few punctate hæmorrhages; on the left side there was found à cyst the size of a hazel-nut, which contained some perfectly sterile fibrin flakes; in the wall of the cyst punctate hæmorrhages.

Dr. Mandlebaum was good enough to examine that portion of the brain, of my case, where the injection was carried out, and found only the slight channel, where the needle penetrated, filled by a small number of red blood-cells.

Experimentally, upon the brains of rabbits, I have also been able to prove to my fullest satisfaction that comparatively large amounts of liquids may be injected into the brain substance without inducing any gross injury, provided, only, that the injection is carried out with the requisite amount of care. For the purposes of this experiment, I have utilized both living and dead rabbits; as injecting fluid I used in the first experiment normal saline solution; but as this disappeared without discoverable trace, I used in the subsequent experiments normal saline solution slightly tinged with methylene blue.

First Experiment.—Large live rabbit; under ether anæsthesia small opening cut into skull and with fine hypodermic syringe injected one cubic centimetre of salt solution. Duration of actual injection four minutes. Rabbit killed after one hour; examination of the brain showed merely a slight subpial hæmorrhage on the surface of the brain; no visible trace of the injected fluid.

Second Experiment.—Same as first experiment, excepting that I tinged the salt solution slightly with methylene blue. Animal died during the operation; quantity injected twenty minims; duration of injection only a few seconds. Autopsy immediately showed laceration of the brain substance, owing to the rapidity of the injection.

Third Experiment.—Same as second experiment, excepting that the duration of the injection was five minutes. Examination after one hour showed a subdural blood-clot about the size of a ten-cent piece, due to the piercing of a larger meningeal vessel; no laceration of the brain substance.

Fourth Experiment.—Same as third experiment, only that the quantity was increased to two cubic centimetres. Examination showed marked œdema at the seat of injection.

Fifth Experiment.—Brain of dead rabbit; otherwise repetition of second experiment; examination showed laceration of brain substance.

Sixth Experiment.—Brain of dead rabbit; otherwise repetition of third experiment; examination negative.

Seventh Experiment.—Brain of dead rabbit; in other respects repetition of fourth experiment; examination showed some laceration of the brain substance.

Brnno [68] has also found that the injection of one cubic centimetre of normal salt solution after trepanation is not productive of the least harm. Judging from these experiments, I am led to the belief that the living brain can stand without harm the injection of small amounts of fluid; but it must be carried out very slowly, as any undue haste will very probably result in more or less laceration.

Uncalled for injury to the brain may also be caused by an inadvertent movement of the head of the patient during the injection, the needle causing a rent in the brain. To obviate this accident, Rambaud [69] has invented a very ingenious needle, which fits tightly into the trephine opening, and in this manner prevents any independent movement on the part of the needle.

This much has been brought out with definite certainty; that the intracerebral injection is practically devoid of danger, provided it is carried out with the required asepsis, and provided the process of the injection itself is not done with undue haste. Bad results, as sepsis, and laceration of the brain substance, with resulting greater or smaller cavities, are due only to errors or insufficient attention to these details.

Regarding the value of the antitoxin treatment in general, it is well to follow Remesoff and Fedoroff's [70] classification, who divide the cases of tetanus treated with antitoxin into four groups:

(1) Cases in which the symptoms are ameliorated at once after the injection, and then gradually but constantly diminish.

(2) Cases in which there is at first no apparent effect on the symptoms, but improve later on.

(3) Cases in which some of the symptoms become more marked after the injection, but no new groups of muscles become involved.

(4) Cases which continue to grow worse and die in spite of the treatment.

It is recommended and strongly urged that the use of antitoxin be begun as soon as possible after the diagnosis of tetanus has been made in a given case; some observers go even so far as to say that the antitoxin can only do good if used within the first thirty-six hours. I have examined the reported cases, also, with a view to determine this question, and find that, though theoretically it may be, nay is, more proper to begin the use of the antitoxin early, in reality, however, it does not appear to make very much difference, as, contrary to expectations, the cases treated very early in the disease, within the first two days, give a higher mortality than the cases treated later on.

No harm whatsoever, at least none of a permanent nature, has been observed after the use of the antitoxin. Very frequently an urticaria or measle-like eruption has been observed, but it usually disappears within a few days, and does not give rise to any untoward symptoms of consequence.

Before concluding this, one might say the most important chapter relating to the treatment of tetanus, it may be well to call attention to the fact that, even with our best intention, a just estimate of the value of the antitoxin treatment cannot be obtained, and this is caused by the unavoidable circumstance that there exist in the market so many different preparations. I have been able to collect cases treated with the following sources: Tizzoni; Behring; Paris Institute Pasteur; New York Board of Health; Massachusetts Board of Health; Parke, Davis & Co.; British Institute of Preventive Medicine; Gibier; Bujwid; Preisz; Boer, etc. Naturally, when the mode of preparation is considered, it is self-evident that the strength of the various preparations must also differ materially in the amount of antitoxin they contain. Another point which must not be lost sight of is that the dosage, for reasons stated above, varies very much, at least it should do so proportionately to the amount of the tangible antitoxins which are contained in the special serum used. Behring[71] has attempted a measure for

the strength of the antitoxin, but it appears to be doubtful whether all preparations can be brought in under this standard.

It is also remarkable that the cases treated in Italy, by Italian observers, with Tizzoni's antitoxin, are all reported as followed by recovery; it is very difficult to explain this discrepancy with reports from other countries.

No one, perhaps, is better aware than I of the fact that it is both difficult and, for that matter, unjust to draw conclusions from statistics when a point like this is under consideration. But, as a matter of interest merely, I have separated the 338 cases reported according to the make of the antitoxin used, and find the following values:

Of 76 cases treated with Tizzoni's antitoxin, 53 recovered and 23 died; of 61 cases treated with Behring's antitoxin, 35 recovered and 26 died; of 39 cases treated with Institute Pasteur antitoxin, 25 recovered and 14 died; of 28 cases treated with British Institute of Preventive Medicine antitoxin, 16 recovered and 12 died; of 27 cases treated with Roux's antitoxin, 9 recovered and 18 died; of 11 cases treated with Tavel's antitoxin, 8 recovered and 3 died; of 10 cases treated with Parke, Davis and Co.'s antitoxin, 8 recovered and 2 died; of 8 cases treated with New York Board of Health antitoxin, 2 recovered and 6 died; of 4 cases treated with Massachusetts State Board antitoxin, 2 recovered and 2 died; of 3 cases treated with Bernese serum antitetanique, 1 recovered and 2 died; of 2 cases treated with Remesoff and Fedoroff's antitoxin, 1 recovered and 1 died; of 2 cases treated with Gibier's antitoxin, 2 recovered and 0 died; of 2 cases treated with Bujwid's antitoxin, 0 recovered and 2 died; of 1 case treated with Preisz's antitoxin, 1 recovered and 0 died; of 1 case treated with Boer's antitoxin, 0 recovered and 1 died; of 63 cases treated with unknown antitoxin, 32 recovered and 31 died.

4. To immunize the body after infection has taken place. If Buchner's view regarding the action of the tetanus antitoxin is accepted, the entire serum therapy of tetanus is

narrowed down to an immunization of unaffected cell territories. Broadly speaking, however, it involves the injection of antitoxin as a prophylactic measure in all wounds where we have reason to suspect the subsequent possibility of tetanus developing. Unfortunately, but little opportunity is offered in practice to carry this plan out, and to judge of the results. It is now carried out systematically at the Prager Gebähranstalt, reported by Pitha,[72] where, after contending with a somewhat extensive epidemic of puerperal tetanus, it was decided to inject prophylactically all patients on whom operative interference for delivery was indicated, and with this treatment only was the epidemic cut short.

Numerous instances, and with almost uniformly good results, are reported in veterinary practice by Nocard [73] and others.

5. To overcome the symptoms induced by the action of the toxins. As the symptoms point largely to an increased reflex irritability of the higher nerve centres, manifesting themselves in spasms and convulsive movements, our first aim should be to exclude all those factors which tend to provoke spasms; this is best done by isolating the patients and by avoiding all unnecessary jars and noises. An item not to be underrated in the symptomatic treatment is also the administration of such remedies which have a tendency to reduce this reflex irritability. Many remedies have been suggested and lauded as of particular value, but have all been more or less discarded. Among those which have a certain value, I will mention particularly the free use of opium and morphine; chloral administered in maximum doses per os, if it can be so administered, or, if that is impossible, per rectum; the bromides, also, in full doses. Of the other remedies which have been used, I will only mention hyoscyamus, paraldehyde, and physostigma.

As a matter of completeness, it may be well to refer here also to two other methods of treatment:

I. The method suggested by Krokiewitz,[74] which consists of the injection of an emulsion of brain substance. Primarily

this method of treatment is based upon the hypothesis, set up by Goldscheider and Flatau (*loc. cit.*), who, as a result of their research, come to the conclusion that "The morphological changes in the nerve cells are the expression of a chemical process, *i.e.*, of the chemical combination of the toxins with the nerve cells. Every nerve cell possesses atom groups, which have a certain affinity for the atom groups of the tetanus toxins and are able to combine with them." Wassermann and Takaki (*loc. cit*) substantiated this hypothesis experimentally; these observers injected into experimentally tetanized animals an emulsion of spinal cord, obtained from a freshly killed animal, to test, if possible, whether the nerve cells of a dead animal also have this affinity for the tetanus toxins, like the nerve cells of a living animal. By this experiment, they have come to the conclusion that every part of the nervous system, particularly the brain of all examined animals, including man, has a definite and positive tetanus antitoxic power; and that the injection of normal brain substance into experimentally tetanized animals has the power to save life, even several hours after an infection has taken place.

Several cases of recovery have been reported by this method by Krokiewitz,[74] [75] Schramm,[76] Kady,[83] Zupnik,[84] and others.

II. The second method aims at the destruction of the toxins circulating in the system by the repeated injection of large quantities of carbolic acid solutions; and known as Baccelli's method. Many cases of recovery have also been reported by this method, as Ascoli,[77] Natoli,[78] Pieraccini,[79] Ziengo,[80] Metelli,[81] and numerous others.

Résumé.

It is exceedingly difficult to make a brief *résumé* from a paper which treats on so many subjects. In concluding, I would merely suggest the following points:

(1) All forms of tetanus are caused by the bacillus of Nicolaier; hence the diagnosis of rheumatic or idiopathic should have no room in our nosology.

(2) The tetanus toxins appear to have a distinct affinity for the anterior horns of the spinal cord, which may be distinctly recognized by Nissl's method of staining.

(3) The cerebrospinal fluid of tetanus patients is more toxic than the blood.

(4) The antitoxin therapy appears to have a distinct beneficial influence upon the course of tetanus.

(5) With the antitoxin treatment the mortality percentage has been reduced from about 90 per cent. to 40 per cent.

(6) Although the use of the serum is a most important factor in the treatment of tetanus, the other recognized therapeutic measures should not be neglected.

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